REMARKS

Claims 1-3, 7, 8, 10-12, and 14 are pending. Claim 14 has been withdrawn from consideration and claims 1-3, 7, 8, and 10-12 are rejected. The rejections are addressed as follows.

I. Rejection under 35 U.S.C. § 112, second paragraph

Claims 7 and 8 were rejected under 35 U.S.C. § 112, second paragraph, on the basis that the phrase "more than one type" is unclear. This rejection has been met by deletion of the phrase "detecting the presence and ratio of more than one type" from claim 7, from which claim 8 depends.

II. Rejection under 35 U.S.C. § 102(b)

Claims 1-3, 7, and 8 were rejected under 35 U.S.C. § 102(b) as being anticipated by Fodor, US 2001/0053519. In the rejection, the Examiner states that the preamble of the claim 1, specifying "a microarray with target probes for detecting drug resistant HBV on a support," merely sets forth the intended use of the claimed microarray, but does not limit the scope of the claims. Regarding Fodor, the Examiner states that this reference teaches an array comprising all possible nucleic acid sequences of any length and, in view of the comprising language in the claims, that Fodor anticipates the claims. More specifically, the Examiner states: "[w]hile Fodor does not specifically discuss probes for detecting point mutations at codons 528... of the HBV DNA polymerase gene, it is a property of the array taught by Fodor that it would comprise probes capable of detecting these point mutations. In view of the comprising language in the claim, the

claimed microarray is not limited to probes that only detect these mutations."

In response, Applicants submit that, according the Examiner's position, any inventions relating to microarrays with target probes having certain mutant sequences for specific useful detection cannot be patented. With respect to the Examiner's statement that the preamble is not limiting, Applicants respectfully disagree, as the preamble requires that the target probes are used for detecting drug-resistant HBV on a support, which clearly limits the microarrays to those that include such probes and which are useful for such detection. In order to be useful for this purpose, there must be some type of design or specification that allows identification of binding to the HBV-related probes. This is not provided by Fodor. The fact that Fodor teaches the possibility of microarrays including completely random sequences does not mean that they teach microarrays including the presently specified probes. Fodor provides no specific teaching as to which sequences among their random sequences could be used for detecting drug-resistant HBV or for controls for such detection, and thus does not teach microarrays that can be used for this purpose. Further, claim 1 has been amended herein to specify in the body of the claim that the claimed microarray can be used to detect drug-resistant HBV. Applicants thus respectfully request reconsideration and withdrawal of this rejection.

III. Rejections under 35 U.S.C. § 103(a)

Claims 10-12 were rejected under 35 U.S.C. § 103(a) for obviousness over Fodor, US 2001/0053519, in view of Kincaid, US 2003/0186310. Applicants respectfully request reconsideration and withdrawal of this rejection.

Fodor is cited for teaching microarrays including probes, as discussed above. Kincaid is

cited for teaching control probes on a microarray. As discussed above, the present claims specify microarrays including probes having particular mutations, which can be used to detect drug-resistant HBV. Microarrays including such probes are not taught or suggested by the cited references. The fact that Fodor indicates that their probes can include all possible nucleic acid sequences of any given length does not mean that they teach the microarrays of the present invention. Even if an array of Fodor happened to end up including a sequence that could be relevant to detection of drug-resistant HBV, the fact that neither Fodor nor the other references provides any teaching as to detection of such HBV makes this rejection untenable. A microarray made according to Fodor would not be useful for detecting drug-resistant HBV, as there would not be any information in such a microarray concerning where such probes would be and thus how they could be monitored for binding. As neither reference even mentions probes for use in detecting drug-resistant HBV, the references cannot support the present rejection.

Further with respect to Kincaid, this reference discloses that "the control probe comprises a sequence of nucleic acids unique to the control probe" in the Abstract, whereas the quality control probes of present invention may have the same sequence as the target probes or arbitrary sequences as specified in claim 11. In addition, the control probe of Kincaid acts as a stilt essentially extending the oligomer test probe away from the surface of the microarray, whereas the quality control probes of the present claims do not extend the target probes, but rather are mixed with the target probes. The control probes of Kincaid also need control-specific target materials, after hybridization therewith a control signal indicative is interrogated, as described in Abstract, while the quality control probes of the present claims do not need any control-specific target materials and hybridization therewith.

Applicants further submit that a central feature of the present invention is to include all HBV mutations related to drug resistance, and this is not taught or suggested by the prior art.

In view of the above, Applicants respectfully request reconsideration and withdrawal of the rejection over Fodor, in view of Kincaid.

Claims 1-3 were rejected under 35 U.S.C. § 103(a) for obviousness over Vernet, Virus Research 82:65-71, 2002, in view of Liu et al., Antiviral Chemistry & Chemotherapy 13:143-155, 2002. Applicants respectfully request reconsideration and withdrawal of this rejection.

Vernet is cited for teaching the potential use of DNA chip technology in the field of clinical virology and diagnostics such as, for example, in genotypic resistance tests, and further that resistance mutations in the genome of HBV have been described. The Examiner further notes that Vernet does not disclose probes for detecting point mutations at codons 528, 529, and 514 of domain B, and at codons 522, 548, and 555 of domain C of the HBV DNA polymerase gene. The Examiner then cites Table 2 of Liu for teaching certain point mutations in HBV DNA polymerases and their association with drug resistance. The Examiner further states that it was well known in the art that probes designed for a specific mutation could be used in order to detect that mutation, and that those of skill in the art would have been motivated to put such probes on a microarray in view of known benefits of microarray technology.

In response, Applicants submit that the microarrays of the present claims include all HBV mutations associated with drug resistance, and such microarrays are not taught or suggested in the prior art. In particular, the microarrays must include target probes that include the nucleotide sequences of point mutations at codons 528, 529, and 514 in domain B, and at codons 552, 548, and 555 in domain C, and/or codons 528 and 529 in domain B and at codon 555 in domain C.

Thus, it is clear that the claimed microarrays must include a probe including a mutation in codon 529. Liu does not teach that codon 529 includes a mutation. Rather, the only information concerning codon 529 in Table 2 of Liu is that "A" is the consensus wild type sequence at this position. Thus, even if Vernet and Liu were properly combined to make the present rejection (which Applicants do not admit), the combination of these references does not teach or suggest a required element of the present claims: a microarray including a probe having a mutation in codon 529. This rejection should therefore be withdrawn. Claims 7 and 8 were rejected under 35 U.S.C. § 103(a) for obviousness over Vernet, Virus Research 82:65-71, 2002, in view of Liu et al., Antiviral Chemistry & Chemotherapy 13:143-155, 2002, and further in view of Anderson, US 2003/0040870. Applicants respectfully request reconsideration and withdrawal of this rejection.

Vernet and Liu are discussed above and, as discussed above, this combination of references cannot support a rejection of the present claims for obviousness. Claims 7 and 8 specify the presence of control probes in the microarray of claim 1, and Anderson is cited for teaching negative control probes. Anderson does not teach that a mutation in codon 529 can result in drug-resistance, not to mention a probe including a mutation in codon 529, and thus Anderson does not make up for the deficiencies of Vernet and Liu in supporting an obviousness rejection of the present claims, as discussed above.

Further, with respect to Anderson, the Examiner states: "Anderson teaches negative control probes. For single base changes (such as a SNP) one probe was made to be the complement of the wild type sequence, one probe was made to be the complement of the mutated sequence, and one probe was made to be complement of a different mutation (para 0064)."

However, the quality-control probes described in paragraph 0064 of Anderson are different from the claimed negative control probes, which are not for quality-control, of the present invention. Further, Anderson discloses probes for SNPs, one is the complement of the wild type sequence and the other is the complement of the mutant type sequence. However, the probes for SNPs of Anderson are target probes regardless of whether they are wild or mutant type. In contrast, the negative control probes of the present invention are different from the target probes. As described on page 11 of the present application "[i]n the present invention, in addition to the target probes having nucleotide sequences with which a wild type and a mutant in a codon of a target gene can be detected, negative control probes are constructed by modifying at least one nucleotide of the nucleotide sequence of each of the target probes using a method such as substitution, insertion, deletion, etc. not to be hybridized with target products."

In view of the above, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 7 and 8 over Vernet, Liu, and Anderson.

Claims 10-12 were rejected under 35 U.S.C. § 103(a) for obviousness over Vernet, Virus Research 82:65-71, 2002, in view of Liu et al., Antiviral Chemistry & Chemotherapy 13:143-155, 2002, and further in view of Kincaid, US 2003/0186310. Applicants respectfully request reconsideration and withdrawal of this rejection.

Each of the cited references is discussed above, and claims 10-12 specify that the microarray of claim 1 includes certain quality control probes, which include particular fluorescent labels. This rejection cannot stand, as none of the cited references, alone or in combination, teaches a required element of the present claims: a probe including a mutation in codon 529 of domain B. This rejection should therefore be withdrawn.

CONCLUSION

Applicants submit that the claims are in condition for allowance, and such action is respectfully requested. Although no fees are believed to be due, if there are any charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

Date: December 12, 2008

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